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10/539,440	06/20/2005	Elisabeth Bock	BOCK8	6815

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,440	BOCK ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,8-15,17,18,20,25-43,45,46,48,49 and 55-57* is/are pending in the application.

4a) Of the above claim(s) *9-13,20,25-43,45,46,48,49 and 55-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 5, 8, 14, 15, 17, and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 June 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/09/2007, 06/14/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on 11/13/2007 is acknowledged. The traverse is on the ground that Groups I and II are related inventions under PCT rule 13.1 because the screening method of group II is used to identify compounds which can be used in the modulating method of claim I. Likewise, the molecule design method of group III can be used to identify compounds which can be used. This is not persuasive because the inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features because no special technical features are shared among invention Group I-III.

With respect to the requirement of election of a single FGF receptor and/or a single peptide, Applicants elect SEQ ID NO: 9 with traverse. The traverse is on the ground that under the PCT administrative Instructions, Annex B, paragraph (c), "if the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. Equally, no problem arises in the case of a genus/species situation where the genus claim avoids the prior art". Applicants argue that no showing of a lack of unity has been made.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. The *In re Harnisch* test for unity of invention is applied in the Markush practice. In the instant case, fibroblast growth factor receptors or a variant thereof do not appear to have a substantial structure similarity and a common utility as a whole, restriction to a single sequence is required. While, as shown in Exhibit A provided by Applicants, FGF receptors and some variants thereof share a certain degree of homology, fibroblast growth factor receptors and variants thereof as recited in claim 1 do not appear to have a substantial structure similarity because all FGF receptors do not share a common structure and variants of FGF receptors do not even have a defined structure. Moreover, FGF receptors and variants thereof do not share a common utility. Activation of FGF receptors by different FGF leads to diverse biological response in various cell types (see, e.g., Stauber et al. PNAS 97:49-54, 2000; Powers et al. Endocrine-Related Cancer 7:165-197, 2000).

Likewise, the recited polypeptides set forth in SEQ ID NOS: 2-146 do not appear to have a substantial structure similarity and a common utility as a whole, restriction to a single sequence is required. While showing some degree of homology among some polypeptides, the exhibit B provided by Applicants does not show that the polypeptides set forth in SEQ ID NOS: 2-146 share a common structure, such as a binding domain. Thus, the recited polypeptides set forth in SEQ ID NOS: 2-146 do not appear to have a substantial structure similarity. Moreover, the polypeptides set forth in SEQ ID

NOS: 2-146 do not appear to share a common utility. For example, they do not appear to bind the same FGF receptors and producing same biological responses.

It is further noted that the prior art teach the instantly claimed methods. For example, Skladchikova et al. (*J Neurosci Res.* 57(2):207-218, 1999) teach modulation of NCAM-FGFR interaction with a fragment of FGFR (the FGFR-CAM homology domain or CHD), an anti-FGFR antibody, an anti-NCAM antibody (an antibody against the NCAM-Fn-III 1-2 modules), as well as ATP in low-density hippocampal neuronal cultures (page 212, last paragraph of left column to the 1st paragraph of right column; Fig. 10).

Accordingly, Groups I-III are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept. Thus, unity of invention is lacking and restriction is appropriate.

During a telephone conversation with Applicants' representative, Iver P. Cooper, on January 11, 2008, Applicants argue that the restriction requirement mailed on 09/13/2007 does not require applicants to elect both an FGF receptor and a polypeptide because of the use of the language "and/or". The examiner clarified that election of both a single FGF receptor and a polypeptide is required. In response, a provisional election of FGFR1 was made with traverse. Affirmation of this election must be made by applicant in replying to this Office action.

2. Applicants' preliminary amendment filed upon 04/05/2006 has been entered in full. Claims 1, 4, 5, 8-15, 17, 18, 20, 25-43, 45, 46, 48, 49, and 55-57 are

pending. Claims 1, 4, 5, 8, 14, 15, 17, and 18 are currently under consideration. All other claims are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/13/2007.

Sequence Compliance

3. The amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s): the amino acid sequences shown in Figs. 6, 8, and 10 must be identified with a SEQ ID NO and an amendment directing its entry into the specification must be provided.

Drawings

4. The drawings filed on 06/20/2005 are objected to because the sequences shown in Figs. 6, 8, and 10 are not identified with a SEQ ID NO. The sequences must either be identified in the legends or in the Drawings. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the

appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Information Disclosure Statement

5. The information disclosure statements filed on 06/14/2006 and 07/09/2007 are considered by the Examiner and a signed copy has been attached to the office action.

Claim Rejections—35 USC § 112, 1st paragraph

6 The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 8, 14, 15, 17, and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The elected invention of claim 1 is drawn to a method of modulating the interaction between a FGFR1 or a variant thereof and a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 9. Claim 18 is drawn, in part, to the method of claim 1, wherein said polypeptide comprises a fragment of SEQ ID NO: 9. Claims 8, 14, 15, and 17 depend from claim 1. Claim 1, as written, encompasses any variants or homologues of FGFR1. The claims do not require that the FGFR1 variants or the polypeptides comprising the amino acid sequence of SEQ ID NO: 9 possess any particular structure nor any functional activity.

The instant disclosure does not adequately support the scope of the genus encompassed in the claims. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features

constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the claimed genus of FGFR1 variants and the polypeptides comprising a fragment of SEQ ID NO: 9. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art teach members of the FGF family and their receptors (Powers et al. Endocrine-Related Cancer 7:165-197, 2000; also see Exhibit A provided by Applicants). However, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed FGFR1 variants or their binding polypeptides as being identical to those instantly encompassed.

Due to the breadth of the encompassed genus of FGFR1 variants and their binding polypeptides and lack of the definitive structural or functional features of the encompassed genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the encompassed FGFR1 variants and their binding polypeptides and thus the instantly claimed method.

Claim Rejections—35 USC § 112, 2nd paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 4, 5, 8, 14, 15, 17, and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is indefinite because it recites a broad range or limitation together with a narrow range or limitation. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 15 recites the broad recitation "within the range of Kd 10^{-3}–10^{-11} M", and the claim also recites "within the range Kd 10^{-5}-10^{-8}" which is the narrower statement of the range/limitation.

Claim 18 is indefinite because it recites both an open language "comprises" and a closed language "consist of" in the claim. Moreover, it is

unclear what Applicants intend to mean by "6 to 16 contiguous amino acid residues".

Claim 1 recites "a method of modulating the interaction". It is unclear what else the term "interaction" encompasses besides binding. Since the specification does not define the term, the claim is indefinite. Claims 4, 5, 8, 14, 15, 17, and 18 are rejected as dependent claims from claim 1.

Claim Rejections—35 U.S.C. §102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 4, 5, 8, 14, 15, 17, and 18 are rejected under 35 U.S.C.§ 102(b) as being anticipated by Skladchikova et al. (*J Neurosci Res.* 57(2):207-218, 1999).

Skladchikova et al. teach neural cell adhesion molecule (NCAM) comprising two fibronectin type-III modules (page 208, left column, lines 8-9), which have been demonstrated to induce neurite outgrowth and cell adhesion (page 208, left column, lines 31-32). Skladchikova et al. teach that NCAM interacts with FGFR through CHD located in the second Ig module of the FGFR and a site for recognition of FGFR-CHD is located in the first Fn-III module of NCAM, which necessarily comprises the amino acid sequence of SEQ ID NO: 9.

Skladchikova et al. teach modulation of NCAM-FGFR interaction with a fragment of FGFR (the FGFR-CAM homology domain or CHD), an anti-FGFR antibody, an anti-NCAM antibody (an antibody against the NCAM-Fn-III 1-2 modules), as well as ATP in hippocampal neuronal cultures that necessarily express FGFR1 (page 212, last paragraph of left column to the 1st paragraph of right column; Fig. 10). FGFR antibodies, CHD, and NCAM antibodies all abrogated ATP-stimulated neurite outgrowth (page 212, the 1st paragraph of right column; Fig. 10).

Accordingly, the teachings of Skladchikova et al. meet the limitations of claims 1, 4, 5, 8, 14, 15, 17, and 18.

Claim Objections—Minor Informalities

12. Claims 1, 4, 8, 14, 15, 17, and 18 are objected to because of the following informalities: (i). the unit for Kd is missing at the end of claim 15; (ii). claims 1, 4, 8, 14, 15, 17, and 18 recite non-elected fibroblast growth factor receptors and binding polypeptides. Appropriate correction is required.

13. The prior art made of record in PTO-892 form is considered pertinent to Applicants' disclosure.

The publication of Kiselyov et al. (Structure. 11:691-701, June 2003), which is before the filing date of PCT/DK03//00901, but after the priority date, teaches the instantly claimed methods.

Conclusion

14. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li

RUIXIANG LI, PH.D.
PRIMARY EXAMINER

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January 19, 2008